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☐ 1: J Photochem Photobiol B. 1998 Jul 10;44(2):151-8.

Enhancement of tumour response to photodynamic therapy by adjuvant mycobacterium cell-wall treatment.

Korbelik M, Cecic I.

Cancer Imaging Department, British Columbia Cancer Agency, Vancouver, Canada. mkorbeli@bccancer.bc.ca

Mycobacterium cell-wall extract (MCWE) is a potent non-specific immunostimulant that elicits a local inflammatory response associated with antitumour activity. Tumour-localized administration of MCWE has been examined as an adjuvant to photodynamic therapy (PDT) mediated by the photosensitizers Photofrin, benzoporphyrin derivative monoacid (BPD), metatetrahydroxyphenylchlorin (mTHPC), or zinc (II)-phthalocyanine (ZnPc). A single MCWE treatment, given immediately after light treatment of murine EMT6 tumours, potentiates the curative effect of PDT. A similar enhancement of tumour response to Photofrin-based PDT is obtained with the live Bacillus Calmette-Guerin (BCG) vaccine. Despite differences in the kinetics/intensity of damage induction to tumour microvasculature and other characteristics underlying the mechanism of antitumour activity of Photofrin, BPD, mTHPC and ZnPc, there appear to be no marked differences in the therapeutic benefit of adjuvant MCWE therapy combined with the PDT mediated by these various photosensitizers. This may be related to the fact that MCWE elicits a wide range of immunomodulatory effects that could amplify and sustain the inflammatory/immune responses triggered by PDT. The enhancement of inflammatory effector cell activity is indicated by the increased infiltration of neutrophils and other myeloid cells at the expense of malignant cells found in the MCWE plus mTHPC-based PDT treatment group compared to the PDT-only group.

PMID: 9757597 [PubMed - indexed for MEDLINE]

☐ 1: J Biol Response Mod. 1983;2(4):321-42.

Related Articles, Links

Clinical immunotherapy trials of bacterial components derived from Mycobacteria and Nocardia.

Vosika GJ.

Preparations of oil-attached mycobacterial components have been used in place of viable bacille Calmette-Guerin (BCG) in animal models and humans as a cancer immunotherapeutic agent. Most preparations consist of the isolated mycobacterial cell wall or cell wall skeleton attached to oil. Cord factor (trehalose dimycolate) has also been included in some preparations. In animal models, such preparations given intralesionally, systemically, or as a vaccine can cause regression of disease and establish tumor-specific immunity. Trials in humans have utilized oil-attached mycobacterial components given intralesionally, intradermally, intrapleurally, intraperitoneally, intravenously, and as an ointment. The major toxicity has been fever, chills, and local inflammation and/or abscess formation. An increase in the white blood count and lymphocyte count has been observed. An increase in liver function test was reported in a minority of patients. Given intralesionally, these preparations cause regression of the injected lesion, regression of noninjected cutaneous and visceral disease, and the apparent establishment of a tumor-specific immune response. Administered intrapleurally and intraperitoneally, there is a response and a clearing of malignant cells in approximately 50% of cases. Given intravenously, oil-attached cell wall skeleton and trehalose dimycolate can eradicate pulmonary disease. Used as an ointment, the preparations have been effective in mycosis fungoides and Kaposi's sarcoma. These reagents demonstrate definite single-agent activity. This was most prominent in patients who were immunocompetent and who had immunogenic tumors such as malignant melanomas. The reagents represent potent immunotherapeutic agents with acceptable toxicity. Further trials of these and subsequent refined preparations are warranted.

Publication Types:
- Clinical Trial
- Review

PMID: 6358421 [PubMed - indexed for MEDLINE]

1: Ann N Y Acad Sci. 1976;277(00):228-38. Related Articles, Links

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Related Resources

Immunotherapy with nonviable microbial components.

Ribi E, Milner KC, Granger DL, Kelly MT, Yamamoto K, Brehmer W, Parker R, Smith RF, Strain SM.

Structural components of microorganisms have been studied for immunopotentiating effect with the aid of transplantable (line 10) tumors in syngeneic guinea pigs. Microbial components were associated with oil droplets, suspended in Tween-saline, and injected intralesionally. BCG cell walls, given in this way, produced regression and cure of 50-60% of established tumors, as did viable BCG. Lipid extraction markedly reduced the tumor-regressing potency of cell walls, but P3, a trehalose mycolate present in the extract, restored full activity to the cell wall residue. P3 alone was nonsensitizing and had no antitumor activity, but it enhanced the latter property of various other microbial products. For example, the cure rates produced by cell walls of M. tuberculosis, M. bovis, M. phlei, or M. smegmatis were enhanced from 20-60% to as much as 90% by addition of P3. P3 also conferred antitumor activity on products from unrelated microbes, such as cell walls of E. coli, and in combination with endotoxins from rough Re mutant salmonellae, it produced cure rates of up to 93%. These results suggest that P3 is essential to the immunopotentiating activity of mycobacteria and that it may be broadly applicable in immunotherapy of cancer with microbial agents.

Publication Types:
- Review

PMID: 187099 [PubMed - indexed for MEDLINE]

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1: J Photochem Photobiol B. 1998 Jul 10;44(2):151-8.

Related Articles, Links

ELSEVIER FULL-TEXT ARTICLE

Enhancement of tumour response to photodynamic therapy by adjuvant mycobacterium cell-wall treatment.

Korbelik M, Cecic I.

Cancer Imaging Department, British Columbia Cancer Agency, Vancouver, Canada. mkorbeli@bccancer.bc.ca

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PMID: 9757597 [PubMed - indexed for MEDLINE]

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☐ 1: Acta Leprol. 1989;7 Suppl 1:55-8.

Related Articles, Links

Serologic and immunocytochemical analysis of the Mycobacterium avium cell envelope.

David HL, Thorel MF, Frehel C, Rastogi N.

Unite de la Tuberculose et des Mycobacteries, Institut Pasteur, Paris, France.

Whole cell sonicates of Mycobacterium avium ATCC 15769, and subcellular fractions (CYT, cytosol; CM, cytoplasmic membrane; CWS, delipidated cell wall skeleton; OL, native lipids; and SDS, sodium dodecylsulfate extract of whole cells) were injected into rabbits to produce corresponding antisera. Immunoelectrophoretic analysis and immunochemical observations using electron microscopy showed that few of the antigens synthetized intracellularly were exported and located in the bacterial outer layers, and that the outer layers contained wall specific antigens possibly in situ assembled.

PMID: 2504006 [PubMed - indexed for MEDLINE]

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1: Vet Microbiol. 1988 Aug;17(4):323-34. Related Articles, Links

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Influence of immunomodulatory agents on bovine humoral and cellular immune responses to parenteral inoculation with bovine rotavirus vaccines.

Archambault D, Morin G, Elazhary Y.

Faculty of Veterinary Medicine, Department of Pathology and Microbiology, St Hyacinthe, Que., Canada.

Sodium diethyldithiocarbamate (DTC), mycobacterium cell wall extract (MCWE, Regressin), killed Corynebacterium parvum (C. parvum, Immunoregulin) and muramyldipeptide (MDP) were each combined with purified, live bovine rotavirus and inoculated into 3 month-old Holstein-Friesian calves in order to examine their ability to potentiate specific humoral and cellular immune responses. The vaccinated calves were boosted twice at 3 and 6 weeks after initial vaccine inoculation. The rotavirus was administered intramuscularly either in an aqueous suspension or in a water-in-oil (WIO) emulsion, prepared with incomplete Freund's adjuvant (IFA). DTC and C. parvum were given by the intravenous route, while MCWE and MDP were incorporated directly in the rotavirus suspension. Two groups of calves were also vaccinated either with rotavirus and IFA or with rotavirus emulsified in mineral oil and a mannide oleate compound (MOC, Montanide 888). A control group of calves was given phosphate-buffered saline (PBS) solution emulsified with IFA. The different vaccine preparations were then compared by studying the kinetics of serum rotavirus-neutralizing antibody production and of proliferative response by blood lymphocytes following in vitro stimulation with bovine rotavirus. The results showed that: (1) the bovine rotavirus should be incorporated in a WIO emulsion in order to induce a cell-mediated immune response as detected by the rotavirus-specific in vitro stimulation test with blood lymphocytes, and to produce higher neutralizing antibody titers in the serum; (2) the vaccines prepared with the mineral oil-MOC complex or IFA both induced comparable levels of humoral and cellular immune responses. The use of mineral oil and MOC as adjuvant may be preferred to IFA, because of the facility of preparing the vaccine and of the low viscosity of the resulting WIO emulsion: (3) the addition of MDP to the WIO emulsion prepared with IFA resulted in a higher cell-mediated immune response as determined by the in vitro blood lymphocyte transformation index specific for bovine rotavirus.